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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2023-D-0202]

Potency Assay Considerations for Monoclonal Antibodies and Other Therapeutic Proteins Targeting Viral Pathogens; Draft Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft guidance for industry entitled "Potency Assay Considerations for Monoclonal Antibodies and Other Therapeutic Proteins Targeting Viral Pathogens." The purpose of this draft guidance is to provide to sponsors recommendations that assist in the development of monoclonal antibodies (mAbs) and other therapeutic proteins that directly target viral proteins or host cell proteins mediating pathogenic mechanisms of infection. A critical quality control measure for these products is the development and implementation of a potency assay(s) adequate to ensure that each lot is produced consistently with the potency necessary to achieve clinical efficacy and that such potency is maintained over the shelf life of the product. This draft guidance provides detailed recommendations to drug developers with the goal of helping to ensure that drug developers provide adequate information to assess potency at each stage of a product's life cycle.

DATES: Submit either electronic or written comments on the draft guidance by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*] to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance.

ADDRESSES: You may submit comments on any guidance at any time as follows:

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: https://www.regulations.gov. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to https://www.regulations.gov will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on https://www.regulations.gov.
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

Written/Paper Submissions

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in "Instructions."

Instructions: All submissions received must include the Docket No. FDA-2023-D-0202 for "Potency Assay Considerations for Monoclonal Antibodies and Other Therapeutic Proteins Targeting Viral Pathogens." Received comments will be placed in the docket and, except for those submitted as "Confidential Submissions," publicly viewable at https://www.regulations.gov or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday, 240-402-7500.

- Confidential Submissions--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states "THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION." The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on https://www.regulations.gov. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as "confidential." Any information marked as "confidential" will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: https://www.govinfo.gov/content/pkg/FR-2015-09-18/pdf/2015-23389.pdf.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to https://www.regulations.gov and insert the docket number, found in brackets in the heading of this document, into the "Search" box and follow

the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, 240-402-7500.

You may submit comments on any guidance at any time (see 21 CFR 10.115(g)(5)).

Submit written requests for single copies of the draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10001 New Hampshire Ave., Hillandale Building, 4th Floor, Silver Spring, MD 20993-0002. Send one self-addressed adhesive label to assist that office in processing your requests. See the SUPPLEMENTARY INFORMATION section for electronic access to the draft guidance document.

FOR FURTHER INFORMATION CONTACT: Natalia Comella, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 75, Rm. 6648, Silver Spring, MD 20993-0002, 301-796-6226.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled "Potency Assay Considerations for Monoclonal Antibodies and Other Therapeutic Proteins Targeting Viral Pathogens." The purpose of this draft guidance is to provide to sponsors recommendations that assist in the development of mAbs and other therapeutic proteins that directly target viral proteins or host cell proteins mediating pathogenic mechanisms of infection. A critical quality control measure for these products is the development and implementation of a potency assay(s) adequate to ensure that each lot is produced consistently with the potency necessary to achieve clinical efficacy and that such potency is maintained over the shelf life of the product. This draft guidance provides detailed recommendations to drug developers with the goal of helping to ensure that drug developers provide adequate information to assess potency at each stage of a product's life cycle.

This draft guidance applies only to mAbs and other therapeutic proteins regulated by the Center for Drug Evaluation and Research that are designed to bind to viral proteins or their receptors on host cells, inhibit viral entry, and/or elicit Fc-mediated effector function and are subject to licensure under section 351(a) or section 351(k) of the Public Health Service Act (PHS Act) (42 U.S.C. 262(a) or (k)). This draft guidance does not apply to immunomodulatory drugs (e.g., cytokines or cytokine antagonists), vaccines, hyperimmune globulins, gene therapies, cell therapies, and convalescent plasma.

The draft guidance describes approaches that sponsors should use to develop potency assay methods for release and stability that assess comprehensively known or potential mechanism(s) of action of the product. The sensitivity of these methods must be established, for example, to conduct the appropriate laboratory determination of satisfactory conformance to final specifications for the drug product (i.e., demonstrate lot-to-lot consistency). In addition to release and stability methods, other methods that demonstrate the biological function(s) of the product may be needed for characterization and comparability studies. The draft guidance describes methods that sponsors should use to ensure the potency of mAbs and other therapeutic proteins proposed to prevent or treat a viral infection.

In January 2021, FDA published the guidance for industry entitled "COVID-19: Potency Assay Considerations for Monoclonal Antibodies and Other Therapeutic Proteins Targeting SARS-CoV-2 Infectivity" (available at https://www.fda.gov/media/145128/download) to support public health efforts following a declaration, under section 319 of the PHS Act (42 U.S.C. 247d), by the Secretary of Health and Human Services of a public health emergency related to Coronavirus Disease 2019 (the disease caused by SARS-CoV-2) (section 319 public health emergency). The 2021 guidance focuses solely on addressing potency assays as they relate to mAbs and other therapeutic proteins that directly target SARS-CoV-2, and it is intended to remain in effect only for the

duration of the section 319 public health emergency related to Coronavirus Disease 2019. However, FDA believes that many of the recommendations set forth in the 2021 guidance are applicable outside the context of the section 319 public health emergency and are applicable to mAbs and other therapeutic proteins directly targeting any viral surface (glyco)proteins mediating pathogenic mechanisms of infection, not just those that directly target SARS-CoV-2. FDA is, therefore, issuing this draft guidance. In preparing this guidance, FDA considered comments received regarding the 2021 guidance as well as the Agency's experience with SARS-CoV-2 and other viruses.

This draft guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the current thinking of FDA on "Potency Assay Considerations for Monoclonal Antibodies and Other Therapeutic Proteins Targeting Viral Pathogens." It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations.

II. Paperwork Reduction Act of 1995

While this guidance contains no collection of information, it does refer to previously approved FDA collections of information. Therefore, clearance by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501-3521) is not required for this guidance. The previously approved collections of information are subject to review by OMB under the PRA. The collections of information in 21 CFR part 312 for submission of an investigational new drug application have been approved under OMB control number 0910-0014. The collections of information in 21 CFR part 314 for new drug applications have been approved under OMB control number 0910-0001. The collections of information in 21 CFR parts 601 and 610 pertaining to biologics license applications have been approved under OMB control number 0910-0338. The collections of information in 21 CFR parts 210 and 211

pertaining to current good manufacturing practices have been approved under OMB control number 0910-0139. The collections of information in 21 CFR part 11 pertaining to electronic records and signatures have been approved under OMB control number 0910-0303.

III. Electronic Access

Persons with access to the internet may obtain the draft guidance at https://www.fda.gov/drugs/guidance-compliance-regulatory-information/guidances-drugs, https://www.fda.gov/regulatory-information/search-fda-guidance-documents, or https://www.regulations.gov.

Dated: February 27, 2023.

Lauren K. Roth,

Associate Commissioner for Policy.

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